UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/701,257 | 04/11/2002 | Richard Charles Trembath | 3548 P 002 | 7815 |

7590 04/26/2005

Monique A Morneault
Wallenstein & Wagner
311 South Wacker Drive 5300
Chicago, IL 60606-6630

| EXAMINER | |
|---|---|
| SAKELARIS, SALLY A | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 04/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/701,257 | TREMBATH ET AL. | |
| | Examiner | Art Unit | |
| | Sally A. Sakelaris | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1,4-10,12,14-16 and 18-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-3, 11, 13, and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/01 1/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Arguments*

Applicant's election without traverse of Group II, claims 2-13 and 17 drawn to a method of determining the susceptibility of a patient to psoriasis in the reply filed on 10/25/2004 is acknowledged. Applicants further election submitted on 1/21/2005 of the single haplotype consisting of a T at position 619, a G at position 1240 and a C at position 1243 is further acknowledged. It should be noted that claims reading on nonelected haplotypes will not be examined as they are each a patentably distinct invention characterized by a distinct structure and would cause a substantial burden on the office to search and examine every invention as claimed. As a result claims 2, 3, 11, 13, and 17 are herein examined as only they read on the elected group and haplotype per applicants' elections of 10/25/2004 and 1/21/2005.

### *Priority*

Acknowledgement of claim to foreign priority of United Kingdom Application, 9906993.2, filed 3/26/1999 under 35 U.S.C. 119(a)-(d) has been made, however applicant should note that the certified copy of this foreign priority document has not yet been received and as a result the claim to foreign priority under the same has not yet been granted. For examination purposes, the present priority date is 3/27/2000.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. Claim 17 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 2, 3, 11, 13, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 2, 3, 11, 13, and 17 are indefinite over the recitation of "the S gene". The phrase lacks antecedent basis as claim 2 makes no prior reference to a S gene or the gene to which "the S gene" refers. It is therefore unclear to which gene a comparison is being made and appropriate correction is required.

B. Claim 17 provides for the use of "the S gene", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 2, 3, 11, 13, and 17 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

Claims 2, 3, 11, 13, and 17 are broadly drawn to a diagnostic test method for determining the susceptibility of any patient, human or animal, to psoriasis through a broad comparison of the entire "S gene", for which there is no provided SEQ ID NO: or sequence incorporation by reference, between any patient and any other sequence of the s gene, also with no SEQ ID NO: or sequence incorporated by reference. As will be further discussed, there is no support in the specification, prior art, or post-filing date art for this type of method. The invention is an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The unpredictability of the art and the state of the prior art

The specification teaches no SEQ ID NO: nor includes any incorporation by reference to provide a structure of the S gene. The specification merely recites papers such as Zhou et al. and Chaplin et al. and the accession number L20815 as containing examples of the "S gene" there is no official incorporation by reference of any specific sequence in the case. As such there is no teaching of how to use the "S gene", or what the "S gene" actually is. While applicant does provide evidence for linkage to psoriasis for the S gene defined as allele 5 ($p<0.000003$)(Table 3). The specification is void of a teaching that would enable the diagnostic method for use with the entire S gene sequence as no sequence is present. The specification itself lends unpredictability issues involved in the practice of this invention on page 6 in its assertion that "despite being strongly associated with psoriasis, the S gene is not the sole determining factor, a person having allele 5 of the S gene but no family history of psoriasis may be less likely to suffer from psoriasis than a person having allele 5 of the S gene and having family history of psoriasis".

There is a great deal of unpredictability involved in correlating SNPs of the S gene with psoriasis. The prior art exemplifies the uncertainty through Ahini et al.'s(Journal of Investigative Dermatology, April, 1999) Vol. 112, No. 4, pp. 591) teaching that "No association was found between disease(or any subtypes by age of onset) and the S gene polymorphism at position +619 despite its close proximity to HLA-C and the strong linkage disequilibrium between the loci"(pg. 591 paragraph 410). In addition, Ishihara et al.(Tissue Antigens 1996: 48:182-186) also looked at polymorphisms in the S gene and their correlation to Psoriasis. Ishihara et al. detected 9 diallelic polymorphisms in the coding region of the S gene in a Japanese

population and among them 3 polymorphic sites in exon 2 that give rise to AA substitutions. However, they discovered that "when we[they] analyzed association of the S alleles with the patient group, there was no significant difference in the S dimorphic distributions between the total patients and controls. In addition, following the analysis of each of the claimed SNPs(see table 2; 619, 1240, and 1243), they concluded that "the S gene is unlikely to confer the primary predisposition to psoriasis vulgaris"(Pg. 186).

Furthermore, there is a large body of knowledge in the prior art related to polymorphisms in general, and their association with diseases or disease states. The art is highly unpredictable with regard to the functionality of polymorphic sites in genomic DNA. After a screening assay identifies polymorphisms, it is unpredictable whether any such polymorphisms would be associated with any phenotypic trait, such as a disease state or a physiological state. For example, Hacker et al. were unable to confirm an association between a gene polymorphism and ulcerative colitis in a case where prior studies suggested such a relationship would exist since the relationship had been identified in a different population (Gut, 1997, Vol. 40, pages 623-627). Even in cases where an association between a particular gene and a disease state is known to exist, such as with the LPL gene and heart disease risk or the p-globin gene and sickle cell anemia, researchers have found that when using SNP (single nucleotide polymorphism analysis) it was difficult to associate SNPs with disease states or to even identify key genes as being associated with disease (Pennisi, Science, 281 (5384):1787-1789). Finally, in some cases where multiple polymorphisms are identified in a gene, some of these are demonstrated to be disease associated and some are not. Blumenfeld et al. (WO 99/52942) disclose a number of polymorphisms in the FLAP gene. While Blumenfeld et al. were able to demonstrate that some

of these polymorphisms are associated with patients having asthma but some of these are not (see Figure 3). For example, the marker 10-35/390 was demonstrated to be associated with asthma, with a p value of 0.00229, while the marker 10-33/327 was determined to not have a statistical association with asthma (p=0.294). Thus, even for SNPs within the same gene, it is highly unpredictable as to whether a particular marker will be disease associated.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters that would have to be studied to apply this technology to all SNPs within the S gene. First, it would be impossible to perform any experiments since there is no sequence provided for the S gene. But even if there were, there would need to be a sequence for every human or animal patient on which the method intends to be practiced since the claims are not limited to humans alone. Also one must consider (a) the ability of the SNP individually to correlate significantly with psoriasis (b) the ability of various haplotypes to correlate significantly with psoriasis etc. The time table necessary to discover these SNPs and their possible significant associations with psoriasis would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps, but practically is seen as being prophetic as such associations are simply unknown at the present.

Working Examples

The specification has no working examples of any haplotype(s)/ SNPs other than that of allele 5 in the method being claimed but does not include an example with a specific SEQ ID NO: or a sequence for the S gene incorporated by reference.

Guidance in the Specification.

The specification provides no evidence that the disclosed method would be able to be practiced with any SNP in any S gene sequence now discovered or yet to be discovered. The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention in any and all sequences that may exist and are entitled the "S gene". Even if, arguendo, there exists SNPs with the sequence referred to herein of the S gene, there is no significant correlation of these SNPs to psoriasis.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where the use of SNPs to detect disease states is even further unpredictable, the factor of unpredictability weighs heavily in favor of undue experimentation. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

4. Claims 2, 3, 11, 13, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses no SEQ ID NO: that corresponds to their exact S gene sequence presently being claimed. Furthermore, no sequence is officially incorporated by reference into the specification. Page 1 of the specification recites accession number L20815 but also recites deposits including NM_001264, AJ238467, etc. Each sequence is different in length, some are fragments and others are entire cDNAs. Each sequence represents different versions of the S gene or CDSN gene. As a result, the structure that applicant is presently claiming is not described at all. The mere recitation of "the s gene" provides no structural limitation to the claims. For example, since the numbering of each of the delineated sequences on page 1 of the specification is different, it is not apparent what nucleotide is represented at positions 619, 1240, and 1243, as each sequence is numbered differently and may include a different nucleotide at such an arbitrary position. In addition, the genus encompassing all of those sequences of the "s gene causing a predetermined susceptibility to psoriasis: is not only very large but also prophetic. Applicant is not in possession of each and every one of these, undisclosed structures. Applicant is claiming every version of any patient's, human or animal species, "s gene" applicant has provided no sequence from any species. The problem involved in claiming SNPs and multiple variants conferred thereby is evaluated in the revised interim written description guidelines example 11.

Reading these claims as broadly as they are written, one could interpret that the entire human genome be encompassed in claims 2, 3, 11, 13, and 17 with only minimally including any

version of the "s gene". Also there is no teaching of the core structure of the genus of "S gene" members, i.e. the defining characteristic of the S gene that causes the correlatable susceptibility. With respect to claim 11, there again is no provision for what characteristic had by all of the primers makes them "discriminatory" as no reference sequence is provided. A review of the full content of the specification indicates that the sequence of "the S gene" and all aforementioned variations, are essential to the operation and function of the claimed invention. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Without the presence of a SEQ ID NO: by which the "S gene" is represented, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The named ORF is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for isolating and characterizing cDNA sequences from *E. grandis*, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe *E. grandis* cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the specification does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute *E. grandis* cDNA appears in the application. Accordingly, the specification does not provide a written description of the invention of claims 1, 4, and 6-15.

Therefore, none of the sequences encompassed by the claim meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 2, 3, 11, 13, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Ishihara et al.(Tissue Antigens 1996: 48:182-186).

It should be noted in the following art rejection, that the recitation of "a predetermined susceptibility" in claim 2 is being interpreted as being any degree of susceptibility as long as it is predetermined, i.e., it may be no susceptibility at all, as long as it is predetermined. The only requirement seen as existing in the claim is for a predetermined susceptibility of any degree, from none to total.

With regard to claim 2, Ishihara et al. teach:

A diagnostic method for determining the susceptibility of a patient to psoriasis, comprising the steps of:

i) taking a sample from said patient;(63 Japanese patients, pg. 183 left side)

ii) comparing the sequence of the S gene of said patient to that of an S gene causing a predetermined susceptibility to psoriasis(in this case no susceptibility) see subject description section and HLA typing teaching on page 183.

iii) correlating the results of comparison step (ii) to determine the susceptibility of said patient to psoriasis(in this instance, no susceptibility) in their results section on page 184.

With regard to claims 3, 11, and 13 Ishihara et al. teaches the claimed nucleotide positions in exon 2 of the S gene, i.e. T nucleotide at position 619, a G nucleotide at position 1240, and a C nucleotide at position 1243 in their table 2. Furthermore, in Ishihara et al.'s teaching of Table 1, they also anticipate the limitations of claims 11 and 13 requiring primers that amplify the specific SNPs within the S gene and a diagnostic method using the same.

Lastly, with regard to claim 17, the use of the S gene in the manufacture of a diagnostic test for psoriasis is herein taught in Ishihara et al.'s PCR RFLP analysis of the S gene(see for example 184).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally A. Sakelaris whose telephone number is 571-272-0748. The examiner can normally be reached on M-Fri, 9-6:30 1st Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 571-272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SALLY SAKELARIS
4/21/05

JEANINE A. GOLDBERG
PRIMARY EXAMINER
4/22/05